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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/155,982	10/09/1998	FREDERIC KLEIN	032475-001	9420

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EXAMINER	
PORTNER, VIRGINIA ALLEN	

ART UNIT	PAPER NUMBER
1645	33

DATE MAILED: 11/25/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/155,982	Applicant(s) KLEIN ET AL.	
	Examin r Ginny Portner	Art Unit 1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 September 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disp sition of Claims

4)☐ Claim(s) *40-83* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) *40-42,44,48,50,51,54-63 and 75* is/are allowed.

6)☐ Claim(s) *43,45-47,49,52-53, 64-74, and 76-83* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Claims 1-39 have been canceled.

New claims 40-83 have been submitted.

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on September 11, 2003 has been entered.

Allowable Subject Matter

2. Claims 40-42, 44, 48, 50-51, 54-63, 75 define over the prior art of record and therefore define allowable subject matter.

Claim Rejections - 35 USC § 112

3. Claims 45-47, 52, 64-73 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 45-47, 52, and 64-73 recite the phrase "detecting any product formed", which defines a genus of products that could be formed in an antigen/antibody immunoassay. Dependent claim 47, depends from claim 45, defines one of the types of products formed in an antigen/antibody reaction is a non specific antigen/antibody product. The scope of claims 45-46 and 64-73 is directed to a genus of methods that include the utilization of non specific antigen/antibody reactions for the detection (see Example 5, page 22, instant specification) and diagnosis of an infection by Taylorella equigenitalis. The instant specification does not describe, nor enable the instantly claimed genus of methods which detect any product formed in an antigen/antibody assay, which would include non-specific reactions in a method to diagnose T.equigenitalis infection. The instant specification does not describe, nor provide guidance on how to utilize non-specific antigen/antibody reactions to accurately detect and diagnose T.equigenitalis infection. The specification does not provide original descriptive support for detecting any product in a method for detecting and diagnosing Taylorella equigenitalis infection. The broad recitation of the phrase "any product" defines a genus of products, the genus not having been described in the instant specification. While the specification does provide support for the phrase "detection of any antigen-antibody type reaction product formed (see page 6, lines 11-18)", the antigen/antibody complex being specific and directed to T.equigenitalis (see instant specification page 6, line 12) ", the instant specification does not provide original descriptive support for a genus of methods that use <u>any product formed</u> in an immunoassay of the antigen/antibody type that is not a Taylorella equigenitalis antigen/antibody complex. Any level of antigen/antibody binding is taught not to be indicative of the presence or absence, or diagnosis of Taylorella equigenitalis, as cross reactive antigens

between various bacteria are known to exist between Taylorella and other species of bacterium (see instant specification page 3, lines 27-32). The monoclonal antibodies are not required to specifically immunoreact only with Taylorella equigenitalis and therefore could and would produce non-specific products, due to non-specific binding of the antigen/antibody type. Claims 45-46, 64-73 recite a combination of claim limitations that do not evidence original descriptive support in the instant specification, and therefore recite New Matter.

4. Claim 43 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant specification has not described a genus of methods of obtaining monoclonal antibodies by screening culture supernatants with a fragment or fragments of a 150 kDa T.equigenitalis protein. While the specification evidences original descriptive support for the term "fragments", the fragments are directed to antigen binding fragments of monoclonal antibodies (see page 5, lines 25-26) and fragments of T.equigenitalis bacterium (see page 6, lines 8-9) which would be the 150 kDa protein which immunoreacted in an immunoblot with the monoclonal antibodies of the invention. No original descriptive support for specific subfragments of the 150 kDa protein have been described, nor utilized in a method of obtaining monoclonal antibodies. What has not been described has not been enabled. Removal of the phrase "or a fragment thereof" from the screening step of instant claim 43, could obviate this rejection.

5. Claims 49, and 79-83 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for compositions that comprise monoclonal antibodies and

antigen binding fragments thereof in combination with an inert vehicle, does not reasonably provide enablement for the utilization of any monoclonal antibody , or combination of monoclonal antibodies as a pharmaceutical composition for the prevention of or treatment of preexisting Taylorella equigenitalis infection. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The instant specification discloses a number of monoclonal antibodies that specifically immunoreact with Taylorella equigenitalis antigens, but the nature of the antigens relative to disease progression has not been disclosed. While the instant specification has enabled compositions of monoclonal antibodies for the detection, identification and diagnosis of Taylorella equigenitalis, the utilization of any single monoclonal, monoclonal fragment, or combination of monoclonal antibodies or their fragments for a realized therapeutic effect upon administration to any patient has not been enabled.

The proteins of the instant specification have been isolated and purified, and shown to be immunoreactive with the monoclonal antibodies of the instant invention, and while surface associated, no single epitope, or epitopes have been described to be associated with establishment of infection, or associated with eradication of pre-existing infection, nor that the monoclonal antibodies been shown to evidence opsonic, bacteriocidal activity.

A single monoclonal antibody evidences a homogenous immunoreactivity directed against a single sequence of about 3-10 amino acids (protein epitope), or in the case of a lipopolysaccharide (LPS) a single conformational epitope defined by the lipid and/or sugar components of the antigen. No specific peptides or LPS epitopes have been described that are

responsible for establishment of infection, and no pharmaceutical compositions of antibodies that inhibit the binding of single epitopes, nor a combination of epitopes to which the claimed monoclonal antibodies specifically bind, on the surface of Taylorella equigenitalis have been described or shown to be effective in the treatment or prevention of Taylorella equigenitalis infection.

Immunotherapy is not always protective. Boslego et al (1991), utilizing antibodies directed against a known venereal disease causing pathogen virulence factor, sought to inhibit establishment of infection, but found the antibodies to have no protective effect (see page 212, col. 2, entire column, especially paragraph 4). At page 217, col. 1, paragraph 3, Boslego et al goes on to say, that monoclonal antibodies, though specific for the antigen to which they bind, lack bactericidal activity and fail to protect against infection upon challenge. None of the disclosed monoclonal antibodies have been shown to evidence any bactericidal activity in any accepted in vitro or in vivo model of Taylorella equigenitalis infection.

Therefore, the claimed compositions are only enabled for a scope of the claimed invention, as the person of skill in the art would be required to de novo, determine and identify an epitope or combination of epitopes to which monoclonal antibodies would specifically bind and also function as a pharmaceutical composition. This rejection could be obviated by amending the claims to recite --A [pharmaceutical] composition--

6. Claims 45, 46, 52, 64-73, 74, 76-78 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 45 recites the phrase "method of identification of a bacterium of the species Taylorella" and utilizes an antibody that "recognizes a 150 kDa T.equigenitalis protein". The detecting step of claim 45 does not correlate with the preamble of the method, as any product, albeit specific or non-specific is being claimed; the method of identification is not distinctly claimed as the antibody is not required to specifically detect T.equigenitalis without cross reactivity, as the antibody is functionally defined in claim 40, from which claim 45 depends to merely recognize the protein, and what is detected is any product, and not a specific T.equigenitalis antigen/antibody complex. In light of the prior art and the instant specification teaching that cross reactive antigens exist between Taylorella and other pathogenic bacteria, the method of claim 45 does not distinctly claim a combination of methods steps that would result in the identification of Taylorella. The method does not recite a complete method as no correlation between the product detected and the recited intended us of the method as been set forth in the claim. A correlation step would be a critical element to be carried out, when cross reactive, false positive producing antigens exist in the art of Taylorella equigenitalis identification methods.

Claims 46, 64-73, for the same reasons set forth above for claim 45, are also incomplete methods, as detecting any product, would not define means for diagnosing or identifying the presence or absence of Taylorella equigenitalis infection. No correlation step between the product detected and the recited intended use of the claimed methods is clearly set forth in the claims.

Claim 52 recites the phrase "the non antigen-antibody reaction is blocked" and depends from claim 47 which recites the phrase "blocking the non antigen-antibody reactions". Claim 47

recites the plural of the tense "reactions" and claim 52 recite the term in the singular "reaction". Amendment of claim 52 to recite a consistent tense is requested. –wherein the blocking comprises saturating of the specimen with serum from which anti-T.equigenitalis antibodies have been removed.—

Claims 64-69 are method claims which recite the phrase "an effective quantity of the monoclonal antibodies" and depend from a prior claim which recites a plurality of monoclonal antibodies species, but which monoclonal antibody or antibodies are being utilized in the claimed methods is not clear. Claim 69 recites the phrase "a monoclonal antibody" and depends from claim 41 which recites a plurality of monoclonal antibodies with multiple binding specificities based upon the multiple antigens recited in claim 41. What is/are the binding specificities of the antibodies utilized in the claimed methods? The method utilizes a composition that does not require the presence of monoclonals that bind to the different antigens recited in the prior claim; the scope of the methods utilize a composition of a different, broader in scope than the compositions set forth in the claim from which they depend as the combination of antibodies is not required in the instant methods.

Claims 71 and 73 recite the phrase "a monoclonal antibody" and depend from claims 54 and 59, respectively, which recite a plurality of monoclonal antibodies. The antibody used in the method of either claim 71 and 73 is not the composition of more than one monoclonal antibody of either one of claims 54 or 59; the methods utilize compositions broader in scope than the compositions from which the methods depend. The invention is not distinctly claimed.

Claims 74, 76-78 recite the phrase "the monoclonal antibodies or fragments" and depend from a prior claim that recites multiple monoclonal antibodies with very different binding

specificites. Which of the monoclonal antibodies from the prior claim composition are included in the kit?

Claim Rejections - 35 USC § 102

7. Claims 64,66-69, 71-73 are rejected under 35 U.S.C. 102(b) as being anticipated by Akuzawa et al (1996).

Akuzawa et al disclose the instantly claimed invention directed to a method of identifying, or diagnosing the presence of Taylorella equigenitalis in a sample, the method comprising the steps of:

Bringing a monoclonal antibody (monoclonals referred to as NA-1 and NA-2, see English translation paragraph 3) into contact with a sample (equine uterine sample (see last full sentence of paragraph 3, and protein components of T.equigenitalis K-188 strain, paragraph 3), and

Detecting any product formed of the antigen/antibody type ("exhibited a strong reactivity in the 28-44 kDa range" and "reacted with heat treated antigens" recognizing "polysaccharide or LPS components of the outer membrane") .

The monoclonal antibodies did not react with other equine uterine bacteria, thus defining a method of identifying T.equigenitalis, as well as a diagnostic method. Inherently the reference anticipates the instantly claimed methods that utilize any monoclonal antibody effective to form a reaction complex between a Taylorella equigenitalis antigen and the monoclonal antibody

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ginny Portner whose telephone number is (703) 308-7543. The examiner can normally be reached on 7:30-5:00 M-F, alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (703)308-3909. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703)308-0196.

Vgp
November 19, 2003

LYNETTE R. F. SMITH
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